Thirds &

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June 18, 1993

Dr. Joshua Lederberg The Rockefeller University 1230 York Ave. New York, NY 10021-6399

Dear Josh,

Thanks very much for reading my paper. I'd hoped you would "resonate" with it, and as for seeking "other perspectives", they're what I want to correct. In any case I have sampled many such and have been especially disappointed by medical geneticists who prefer to pursue parochial interests, but - as you point out - they are what pay the bills. Still, everyone agrees reform in medical education is needed and very little other than tinkering is offered. I'm convinced that something like what I have outlined is inevitable; indeed is already happening in the subtle ways that great reforms often do. That is, a climate has to be prepared before things happen with a rush. So I intend to do what I can to push the idea that disease is a natural outcome of the mechanisms of evolutionary change - both biological and social, as well as of their different rates of change.

Thanks too for the reprints, most of which I had seen. The recent JAMA paper was especially helpful. As for the paper by Nesse, I agree that panic and anxiety are generally useful but he doesn't say that in some people these behaviors are inappropriate and destructive (not that he doesn't know that). His approach is typological and neglects individual variation, one of the cardinal sins of today's medical education. Nesse and Williams' aim is to demonstrate that some aspects of disease, or of behavior, represent evolutionary adaptation. That's fine, but I want doctors to be aware that the endowment with which patients begin life has an evolutionary history and that all of the expressions of disease are traceable in one way or another and in some degree, to that history. We are, after all, human to begin with, and then each of us is our own unique self. So this biological history is observable in both immediate responses to the environment and over the lifetime. We have to ask why diseases vary in frequency, in predilection for sex, in intensity of expression, in age at onset. We're very good in medicine at answering questions about how things happen, but its the answers to the why questions that draw the "burden" of the facts together into coherent explanations. Obviously I believe that a strong injection of Ernst Mayr's population thinking is what's needed. We're getting pretty good about recognizing genetic susceptibility, but then we perceive the susceptibility

Page 2 June 18, 1993

as representative of a new group and fail to detect the uniqueness of the individuals therein.

So what I want to see is a <u>synthesis</u> of information to make sense of the dispersive influence of the information overload, and a logic of disease, if cogently assembled and presented, can do just that. If some such logic is woven into the curriculum to replace the principles of the body as a machine, the student will have a set of rules that not only embrace all disease but demonstrate the wisdom of displacing the primary care physician's attention from individuals only, to families wherein prevention of disease can logically be seen to be the principal aim of medicine.

It's my opinion that although people like yourself can be, and have been, enormously helpful, the reform has got to come from within. And there are two sides to it. Physician educators have got to stop perceiving information discovered by biologists as useful only in exposing pathogenesis and in the design of treatment, and begin to think of it as explaining how each particular patient got to the doctor in the first place. And biologists engaged in medical education could help most by giving some emphasis to individuality. For example, I sat in on the beginning course in immunology a few years ago, and although the course was dominated by the genes that specify the molecules, I heard nothing at all about individual variation in those genes (even somatic mutation was treated as if everyone was the same), until a physician appeared to talk about immunodeficiencies, and he was pretty categorical about his diseases too. So the student doesn't get the message from the start.

You ask about Dubos and Dobzhansky. I have most of Dubos' books and Dobzhansky's <u>Mankind Evolving</u> too. Both, I have no question, have influenced me in arriving at the views I express and I should cite them. If I did not it's because I take their lessons as read - nothing in biology does make sense except in the context of evolution, and in the book I am working on I'll pay more direct attention to them.

"Man is a man made species" sounds like Medawar to me, but could as well derive from Lederberg. I once "thought up" the aphorism, "Genes propose, experiences dispose", but found it in something Medawar wrote.

Thanks again for your thoughts and attention.

With best regards,

Barton Childs, M.D.

P3. Thanks again. I really do affreciate your taky The time to wood my paper or comment in it.